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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,350	12/29/2000	Stephen M. Coutts	252312005706	1391

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/753,350	COUTTS ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-25 and 28-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25 and 28-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/27/06; 6/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 22-25 and 28-68 are pending.

2. The rejection of claims 22-25, and 28-68 under 35 U.S.C. 103(a) as being unpatentable over US Pat No 5,268,454 (filed Feb 8, 1991; PTO 892) in view of US Pat 5,276,013 (filed July 15, 1992; PTO 892) is hereby withdrawn because this application is filed 12/29/200, which is after November 29, 1999, and applicants provide evidence that the subject matter of the reference patents and the claimed invention were, at the time the invention was made, owned by or subject to an obligation of assignment to the same person.

3. In view of the amendment filed 6/5/06, the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 45 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of any conjugate formed by at least two analog molecule of any "unidentified immunogen" associated with any antibody mediated autoimmune disorder conjugated to a chemically defined valency platform as set forth in claim 45.

The specification discloses only conjugates comprising at least two immunogens associated with antibody mediated pathology from thyroiditis (thyroglobulin), stroke (cardiolipin), male infertility (α-sperm), myasthemia gravis (acetylcholine receptor), rheumatic fever (carbohydrate complex), allergen, Rh hemolytic disease (D immunogen) that lack T cell epitope and conjugated to polyethylene glycol (valency platform) through a diamino or triamino functional group that provides branched groups and attachment sites at the termini of the valency platform as shown on page 31 of the specification.

With the exception of the specific immunogen associated antibody mediated pathology for the claimed conjugate, there is insufficient written description about the structure associated with function of any and all compound unidentified immunogen associated with any antibody-mediated autoimmune disorder for the claimed conjugate. This is because the structure or the amino acid sequence of the immunogen is required to make the analog that lacks T cell epitope for the claimed conjugates.

The specification discloses only the specific conjugate comprising the specific identified immunogens lacking T cell epitope from the specific antibody mediated autoimmune disease conjugated to a chemically defined valency platform molecule, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of compound to describe the genus of unidentified immunogen in the claimed conjugate. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 6/5/06 have been fully considered but are not found persuasive.

Applicants' position is that instant claim 45 recites the same language as claim 19 of the US Pat No. 6,060,056. The specification teaches how to select analog molecules that bind specifically to antibodies which the T cell-dependent immunogen binds specifically (see page 26-27 and 27-28 of specification). The specification also teaches how to select for those analogs that lack T cell epitope (see specification paragraph bridging pp.26-27 and pp.27-28). Thus, one of skill in the art can select appropriate analog molecules of an immunogen without knowing the identity, such as the structure, of the immunogen.

In response, every patent is examined on its own merit. With respect to the argument that specification teaches how to select analog molecules that bind specifically to antibodies which the T cell-dependent immunogen and how to select analogs that lack T cell epitope, it appears that applicants argue enablement, not written description. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is,

for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). Without the structure of analog molecules of the unidentified immunogen, the specification merely asks one of skill in the art to come up with the structure of such unidentified immunogen, the corresponding analog molecules to said unidentified immunogen then conjugated to a chemically defined valency platform molecule for the claimed conjugate.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claim 45 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "*unidentified* immunogen" in claim 45 is ambiguous and indefinite. One of ordinary skilled in the art cannot appraise the metes and bounds of the claimed invention.

Applicants' arguments filed 6/5/06 have been fully considered but are not found persuasive.

Applicants' position is that when analyzed in light of the application disclosure, claim 45 defines with a reasonable degree of particularity the invention claimed.

In response, if the immunogen associated with autoimmune disorder is unidentified, then the conjugate comprising at least two analog molecules of said unidentified immunogen and the chemically defined valency platform molecule is even more ambiguous. One of ordinary skilled in the art cannot appraise the metes and bounds of the claimed invention.

8. The filing date of the instant claims is deemed to be the filing date of parent application USSN 08/118,055 filed 9/8/1993. Priority application USSN 07/914,869 filed 7/15/02 does not provide a written support for the specific conjugate of inducing specific conjugate formable by the conjugation of at least two analog molecules of the immunogen selected from carbohydrates, lipids, oligosaccharides, polypeptides, peptides, proteins, glycoproteins or lipoproteins and

chemically defined valency platform molecule comprises branching groups, provided by attachment sites located at termini of the valency platform molecule and the valency platform molecule is chemically defined in that the number of branching groups predetermines the number of attachment sites.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 22-25, and 28-68 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent No. 6,060,056. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Claim 1 of the '056 patent recites a pharmaceutical composition comprising a therapeutic effective amount of the conjugate for inducing specific B cell anergy to a T cell dependent immunogen implicated in an antibody-mediated pathology comprising a non-immunogenic valency platform molecule and at least two analog molecules of the immunogen wherein (a) the analog molecules bind specifically to surface antibody on B cells to which the T cell-dependent immunogen binds specifically and (b the conjugate lacks T cell epitopes capable of activity T cells in said individual, and further wherein the analog molecules are selected from the group consisting of peptides, polypeptides, proteins, glycoproteins, lipoproteins, carbohydrates, lipids, and lipopolysaccharides (genus).

Pending claim 22 of instant application recites "A conjugate for inducing specific B cell anergy to a T cell dependent immunogen implicated in an antibody-mediated pathology in an individual suffering from the pathology, wherein said conjugate is formable by the conjugation of: (a) at least two analog molecules of the immunogen, wherein (1) said analog molecules bind specifically to surface antibody on B cells to which the T cell-dependent immunogen binds specifically, (2) the analog molecules lack T cell epitopes, and (3) the analog molecules are selected from the croup consisting of carbohydrates, lipids, lipopolysaccharides, polypeptides, peptides, proteins, glvcoproteins, and lipoproteins; and (b) a chemically defined valency platform molecule, wherein (1) the chemically defined valency platform molecule comprises branching groups; (2) the valency of the platform molecule is provided by attachment sites located at termini of the valency platform molecule and (3) the valency platform molecule is chemically determined in that the number of branching groups pre- determines the number of attachment sites (species).

Although the chemically defined platform molecule in claim 1 of the issued patent does not recite the branching groups, and does not have attachment sites at the termini of platform molecule of instant claims, the chemically defined platform molecule in the conjugate in claims of the '056 patent includes the linear (unbranched groups such as D-lysine) as well as the branching groups at the termini (genus). This is because the '056 patent teaches the valency platform molecule having a polyethylene glycol moiety such as PEG3350 having the formula CH2-(CHOCH2)nCH2- wherein n is approx 74, which is (between o to 300) having a functional group such as the diamino benzoic acid or diamino acid of instant claim 23 located at the termini of the chemically defined platform molecule (see col. 13 through col. 15 of the '056 patent, claims 12-13 of the '056 patent, in particular). The analog molecules in the conjugate in claim 1 of the '056 patent includes at least two analog molecules that lack T cell epitopes and selected from peptides, polypeptides, proteins, glycoproteins, lipoproteins, carbohydrates, lipids, and lipopolysaccharides, an external immunogen, an external immunogen such as drug, allergen, D immunogen associated with Rh hemolytic disease, a self immunogen, a self immunogen that is associated with thyroiditis, diabetes, stroke, male infertility, myasthenia gravis, or rheumatic fever (see claims 1-5 of the '056 patent). The analog molecules in the conjugate of the '056 patent are the same (see claim 6 of '056 patent) or different (see claim 8 of the '056 patent) or unidentified (see claim 19 of the '056 patent, in particular). The conjugate of the '056 patent has four peptides which includes the four analog molecule of instant claim 25 (see col. 20, line 41,

conjugate 5). The '056 patent teaches a pharmaceutical composition comprising the conjugate mentioned above and a pharmaceutically acceptable carrier (see claim 15 of the '056 patent, in particular) and suitable for injection (see col. 6, lines 33-34 of the '056 patent, in particular). The conjugate of the '056 patent wherein the valency platform molecule comprises a triethylene glycol moiety (see claim 13 of the '056 patent, in particular). The antibody mediated pathology in the conjugate of the '056 patent is stroke where the immunogen in the conjugate is cardiolipin (see col. 4, line 57, in particular). Claim 16 of the '056 patent recites a method of inducing specific B cell anergy to a T cell-dependent, which includes the claimed method of inducing of inducing specific B cell anergy to a T cell-dependent in instant claim 48. Claim 17 of the '056 patent recites a method of treating an individual for an antibody-mediated pathology in which undesired antibodies are produced in response to a T cell-dependent immunogen comprising administering a therapeutically effective amount of the composition comprising a therapeutically effective amount of the conjugate comprising a nonimmunogenic valency platform molecule and at least two analog molecules of the immunogen wherein (a) the analog molecules bind specifically to surface antibody on B cells to which the T cell-dependent immunogen binds specifically and (b) the conjugate lacks T cell epitopes capable of activating T cells in the individual, the said method of the '056 patent includes the method of instant claim 49. Claim 39 of the issued patent recites a method of making conjugate comprising forming the conjugates by covalently bonding the analog molecules to the valency platform molecule, which include the method of making conjugate recited in instant claim 50. Likewise, the method recites in claim 18 of the '056 patent includes the method of making the composition recites in instant claim 51. The '056 patent further teaches the valency platform molecule comprises a polyethylene glycol moiety having a molecular weight of about 200 to about 8,000 (see col. 5, lines 62, in particular). The '056 patent also teaches that the analog molecules are attached to valency platform molecule via linker groups such as sulfosuccinimidy-(4-iodoacetyl) aminobenzoate (see col. 6, lines 21-27, in particular). Claim 15 of the '056 patent also recites a pharmaceutical composition comprising the conjugate mentioned above and a pharmaceutical acceptable carrier which includes the pharmaceutical composition recited in instant claims 65-67. The issuance of a patent to instant application (species) would anticipate the claims of the '056 patent (genus).

Applicants' arguments filed 6/5/06 have been fully considered but are not found persuasive.

Applicants' position is that the subject matter defined by claims 1-39 of the 1056 patent does not suggest a conjugate where the valency platform molecule of the conjugate has specific structural and chemical features, such as those claimed in claims 22-25 and 28-68 of the present application. Claim 1 of the '056 patent does not suggest conjugates of a particular valency platform molecule and does not suggest conjugates where the valency platform molecule of the conjugates has the presently claimed features, such as branching groups, attachment sites at termini of the platform molecule and a defined valency. Rather, claim 1 of the '056 patent describes a set of conjugates without regard to the specific chemical and structural features of the valency platform molecule of the conjugate. The chemical and structural features of the conjugates presently claimed would not have been obvious from a claim reciting conjugates without regard to such features. Similarly, dependent claims 2-39 of the '056 patent do not suggest the chemically defined conjugates presently claimed.

In response, a terminal disclaimer is required. The conjugate of a valency platform molecule in claims of the '056 patent is generic to the species of the conjugate of a valency platform molecule that has branching groups, attachment sites at termini of the platform molecule and a defined valency of instant claims. Further, the chemically defined platform molecule in the conjugate in claims of the '056 patent includes the linear (unbranched group such as D-lysine) as well as the branching groups at the termini (genus). A person of ordinary skill in the art reading the patent would conclude that the invention defined in the claim at issue would have been an obvious variation of the invention defined in a claim in the '056 patent. This is particularly true when the valency platform molecule having a polyethylene glycol moiety such as PEG3350 having the formula CH2-(CHOCH2)nCH2- wherein n is approx 74, which is (between o to 300) having a functional group such as the diamino benzoic acid or diamino acid of instant claim 23 located at the termini of the chemically defined platform molecule (see col. 13 through col. 15 of the '056 patent, claims 12-13 of the '056 patent, in particular), which is the same valency platform molecule in instant claims 1 and 33, 34 and 68.

The analog molecules in the conjugate in claim 1 of the '056 patent includes at least two analog molecules that lack T cell epitopes and selected from peptides, polypeptides, proteins, glycoproteins, lipoproteins, carbohydrates, lipids, and lipopolysaccharides, an external immunogen, an external immunogen such as drug, allergen, D immunogen associated with Rh hemolytic disease, a self immunogen, a self immunogen that is associated with thyroiditis, diabetes, stroke, male infertility, myasthenia gravis, or rheumatic fever (see claims 1-5 of the '056

patent). The analog molecules in the conjugate of the '056 patent are the same (see claim 6 of '056 patent) or different (see claim 8 of the '056 patent) or unidentified (see claim 19 of the '056 patent, in particular).

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

14. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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August 18, 2006

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